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without prejudice to Applicants' rights to pursue this claim in other patent application(s). No new matter has been added.

Rejections under 35 U.S.C. § 112, first paragraph Enablement

Claims 12, 25, and 39 stand rejected under 35 U.S.C. § 112, first paragraph for an alleged failure to provide a description sufficient to enable a skilled artisan to practice the claimed invention. Specifically, the Examiner alleges that the specification "while being enabling for ...a nucleic acid encoding an amino acid sequence which is at least 88% identical to SEQ ID NO:26 which promotes survival of neurons, does not reasonably provide enablement for a nucleic acid encoding an artemin amino acid sequence which has at least 8 contiguous amino acids of artemin."

Applicants respectfully assert that claim 39 does not recite this limitation. Claim 25 has been cancelled. Applicants have amended claims 12 to no longer recite "at least 8 contiguous amino acids". Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, first paragraph Written Description

Claims 12, 25, and 39 stand rejected under 35 U.S.C. § 112, first paragraph, for an alleged failure to provide a description "in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Specifically, the Examiner alleges that:

These are genus claims. The claims are drawn to a nucleic acid encoding an artemin amino acid sequence which has at least 8 contiguous amino acids of artemin. The specification and claim do not indicate what distinguishing attributes

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shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions....

Applicants respectfully assert that the claims no longer recite "at least 8 contiguous amino acids".

In the present application, the specification discloses that human artemin and murine artemin share about 88% sequence identity. (Table 1, at p. 18 of the specification). Also, artemin shares less than 50% sequence identity to other GDNF family members. Moreover, the claims require that the claimed polynucleotides have a common function; that is, they encode artemin amino acid sequences that promote survival of neurons. A skilled artisan would reasonably expect that an amino acid sequence that is at least 88% identical to SEQ ID NO:26 and that promote survival of neurons would be an artemin. The limitations, "at least 88% identical to SEQ ID NO:26" and "promote survival of neurons", ensure that any substitutions, deletions, insertions and/or additions in artemin would be minor and would not affect the overall novel feature of the claimed invention. A skilled artisan would reasonably conclude that the Applicants were in possession of the claimed invention at the time of filing. Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 12, 25, and 39 stand rejected under 35 U.S.C. § 112, second paragraph, for an alleged failure to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner alleges that the claims recite a fragment of artemin which is 8 contiguous amino acids long, while also encoding an amino acid which is 88% identical to SEQ ID NO:26.

The claims have been amended to no longer recite "at least 8 contiguous amino acids...".

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Claims 12, 15 and 25 remain rejected as allegedly indefinite in the recitation of the term "biologically equivalent". The Examiner asserts that "a definition of the term 'biological active" [is] not a definition of the term 'biologically equivalent.'" The Examiner states that "it is not clear that the equivalence needs to be function or activity...."

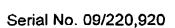
Claims 12 and 15 have been amended to clarify that "biologically equivalent" refers to the biological activity of artemin. As discussed in the previous response, throughout the specification, Applicants describe that artemin functions to promote survival of neurons. (e.g. p. 14, lines 5-9 and p. 15, line 18-21). An amino acid sequence or polypeptide sequence that is at least 88% sequence identical to SEQ ID NO:26 and has the biological activity of artemin promotes survival in neurons. Further, at p. 21, lines 2-5, the Applicants state "[b]y retaining the biological activity, it is meant that the modified polypeptide can bind to and activate GFR\alpha1/RET and/or GFR\alpha3/RET expressed by a cell, although not necessarily at the same level of potency as that of the mature human artemin polypeptide identified herein." Accordingly, Applicants respectfully assert that claims 12 and 15 are clear and respectfully request reconsideration and withdrawal of the rejection.

Claims 12, 15 and 25 stand rejected as allegedly indefinite in the recitation of the term "naturally occurring". Specifically, the Examiner contends that "it is unclear whether....the claim...encompasses...polynucleotides amplified from human cDNA, or only sequences produced by digestion with restriction enzymes of DNA isolated from tissue..., or...all polynucleotide sequences that encode the polypeptide."

Claims 12 and 15 have been amended to no longer recite "naturally occurring."

Applicants submit that all of the claims are clear and definite and respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

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CONCLUSION

Applicants believe that they have overcome or obviated all of the Examiner's rejections and objections. Applicants submit that the application is in proper condition for allowance and respectfully request that such allowance be granted.

Respectfully submitted,

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MARKED-UP VERSION OF AMENDED CLAIMS

12. (Five times amended) An isolated polynucleotide encoding a pan-growth factor which polynucleotide comprises a nucleotide sequence encoding [a naturally occurring] an artemin amino acid sequence [or a fragment thereof that is biologically equivalent to] that has biological activity of artemin, [wherein said fragment has at least 8 contiguous amino acids,] wherein said nucleotide sequence comprises not more than 10,000 nucleotides, and wherein said artemin amino acid sequence is at least 88% identical to SEQ ID NO:26, and wherein said amino acid sequence promotes survival of neurons, and wherein said polynucleotide also comprises a nucleotide sequence encoding a polypeptide containing an active domain of at least one other growth factor from the TGF-β superfamily.

15. (Six times amended) An isolated nucleic acid molecule comprising no more than 10,000 nucleotides, wherein said nucleic acid molecule encodes [a naturally occurring] an artemin amino acid sequence [or a fragment thereof that is biologically equivalent to] that has biological activity of artemin, and wherein said artemin amino acid sequence is at least 88% identical to SEQ ID NO:26, and wherein said artemin amino acid sequence promotes survival of neurons.